UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/782,936	02/14/2001	Vivian E. Mack Strong	19603/4071(CRF-D-2598A)	1665

7590 03/07/2005

Michael L. Goldman, Esq.
NIXON PEABODY LLP
Clinton Square
P.O. Box 31051
Rochester, NY 14603

EXAMINER	
KRASS, FREDERICK F	

ART UNIT	PAPER NUMBER
1614	

DATE MAILED: 03/07/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

HL

Office Action Summary	Application No.	Applicant(s)	
	09/782,936	MACK STRONG ET AL.	
	Examiner	Art Unit	
	Frederick F. Krass	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 November 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,15 and 24-27* is/are pending in the application.

4a) Of the above claim(s) *24-27* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1 and 15* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Written Description Rejection

Claims 1 and 15 were rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement.

This rejection is maintained.

Applicant argues:

> The basis for this rejection is that the specification fails to provide an adequate written description of suitable selective cyclooxygenase-2 ('COX-2') inhibitors. As the U.S. Patent and Trademark Office ('PTO') acknowledges, the specification of the present application identifies benzenesulfonyl compounds like NS-398, celicoxib, MK-0966, and paracoxib as useful selective COX-2 inhibitors. However, the present application also states that suitable inhibitors include those described in WO 99/30721 to Dannenberg et al. ('Dannenberg')(copy enclosed). Pages 3-15 of Dennenberg disclose numerous COX-2 inhibitors. In view of this disclosure, it is clear that applicants had complete possession of the present invention when this application was filed. Accordingly, the rejection under 35 U.S.C. § 112 (first paragraph) should be withdrawn.

The examiner acknowledges that Applicant has described a variety of COX-2 inhibitors, including those incorporated by reference. These are, however, all selective COX-2 inhibitors comprising compounds in which the ratio of the IC_{50} concentration (concentration inhibiting 50% of activity) for cycloxygenase-1 to the IC_{50} concentration for cyclooxygenase-2 is greater than 1. See for example the second full paragraph at page 11 of the instant specification. This is same definition used by WO 99/30721.

By contrast, the broad definition of "COX-2" inhibitor provided by the instant specification is far more expansive. Applicant states at the first full paragraph on page 11:

> The term 'cyclooxygenase-2-inhibitor' or 'COX-2 inhibitor' is used herein to mean <u>any</u> compound that binds to cyclooxygenase-2 enzyme and stops it from functioning. (Emphasis added).

In other words, the term "COX-2 inhibitor" as claimed is inclusive of any compound, known or unknown, which "binds" the COX-2 enzyme to any degree, and which "stops" it from functioning, again to

any degree. Applicant has not provided a written description of, nor provided any guidance for selecting, compounds other than those having the specified IC_{50} ratio values of greater than 1. Accordingly, applicant is not in "complete" possession of the vast number of species potentially falling within the scope of this definition, e.g. peptides, peptide mimetics, inhibitors having RNA-DNA based structure, etc. This position is generally consistent with established precedent; a disclosure of useful species in an unpredictable art is generally adequate only when it is limited to a reasonably circumscribed class. See for example In re Angstadt, 537 F.2d 498, 503 (CCPA 1976).

In light of applicant's arguments, the examiner does agree that the instant specification reasonably provides direction for selecting species falling within the class of compounds having the aforementioned IC_{50} ratios, that class being reasonably circumscribed by the prior art cited by Applicant. Accordingly, the examiner suggests adopting the following language to overcome this ground of rejection:

Claim 1. A method... which comprises administering... a selective inhibitor of cyclooxygenase-2 comprising a compound having a ratio of IC_{50} concentration (concentration inhibiting 50% of activity) for cycloxygenase-1 to IC_{50} concentration for cyclooxygenase-2 of greater than 1, wherein the patient...

Anticipation Rejection

Claims 1 and 15 were rejected under 35 U.S.C. 102(b) as being anticipated by Shoup et al (MEDLINE abstract 1998380907).

This rejection is withdrawn in view of Applicant's amendment and accompanying arguments. As noted therein, the prior art discloses only the treatment of patients (mice) which already have burn sepsis.

Obviousness Rejection (New, Necessitated by Amendment)

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1 and 15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Shoup et al (MEDLINE abstract 1998380907) in view of Spiegelman et al (USP 6,552,055).

As noted in Applicant's response, the primary reference tests the *in vivo* efficacy of the COX-2 inhibitor NS-398 by subjecting mice to a 15% dorsal scald burn plus 1,000 colony-forming units of topical *Pseudomonas aeruginosa* and then administering the COX-2 inhibitor 4-6 hours after the subject is burned and infected. (Shoup, p. 215, abstract; p. 217, left column, 5th paragraph). Thus, the subject already has burn sepsis at the point the COX-2 inhibitor is administered. (Shoup, p. 216, left column, 1st and 2nd paragraph). Accordingly, the primary reference differs from the instant claims insofar as it does not teach using a selective COX-2 inhibitor in a method for prophylaxis of a patient at risk for systemic inflammatory response syndrome and complications thereof, as recited by the instant claims.

It is self-evident to anyone of ordinary skill in the pharmaceutical/medical sciences that if a drug can be used to treat a disease, it is likewise equally useful for prophylaxis of subjects at risk to suffer the disease. Any physician, knowing that a particular patient was at risk to develop a particular disorder, would be motivated by sound medical judgment and practice to administer an agent already known to be therapeutically effective against that disorder thereto in order to minimize the risk of developing the condition. The secondary reference is cited to confirm this assertion and demonstrates the state of the art; it differs from the instant claims insofar as it relates specifically to PPAR-gamma agonists, rather than COX-2 inhibitors. As discussed in detail at the passage spanning col. 17, line 22 to col. 18, line 20 of the patent, it is routine to use animal studies as the basis for human therapy, and to extrapolate from such studies to identify candidate human patients for prophylactic treatment based on known risk factors. See especially col. 18, lines 5-20.

It would have been obvious to have used the COX-2 compounds of the primary reference (recognized therein to be effective in treating burn sepsis) to treat patients at risk to suffer from burns (e.g. individuals occupationally at risk to fire exposure) by implementing the sound scientific methodologies and medical protocols illustrated by the secondary reference, in order to reduce the risk of burn-induced infection in such patients. The motivation to do so would arise from the natural desire of physicians to administer recognized therapies to as wide a range of patients as can be reasonably expected to benefit therefrom.

Action is Final, Necessitated by Applicant's Amendment

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH

shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Frederick F. Krass whose telephone number is 571-272-0580. The examiner's schedule is as follows:

Monday: 10:30AM- 7PM;
Tuesday: 10:30AM - 7PM;
Wednesday: off;
Thursday: 10:30AM- 7PM; and
Friday: 10:30AM-7PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low can be reached at 571-272-0951. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Frederick Krass
Primary Examiner
Art Unit 1614